

REMARKS

Reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

Claims 51 – 55 and 58 have been amended. Claim 51 has been amended by incorporating therein now cancelled claims 61 – 62. The amendments are fully supported in the specification.

The presently pending claims are 51 – 59.

Claims 51 – 62 stand rejected under § 112, 2nd paragraph, for indefiniteness. This rejection is respectfully traversed.

The Examiner asserts that the recitation “consisting essentially of” is vague and indefinite. Applicants wish to point out that this is indeed a defined and accepted transitional phrase according to MPEP 2111.03 Transitional Phrases (R-3). Therefore, the Examiner’s finding is absolutely groundless and the rejection should be withdrawn.

Claim 52 has been amended by rewording the subject matter claimed, particularly by directly referring to cells (b) of Claim 51, in order to overcome the Examiner’s rejection.

Claims 53 and 54 have been amended by rewording the subject matter claimed to provide greater clarity. This amendment overcomes the Examiner’s rejection.

Claim 53 and 54 have been rejected in view of the phrase “in vitro cartilage tissue” that has been deemed to lack antecedent basis. Applicants traverse this assertion, since at par. 0044, it has been clearly stated that the three-dimensional matrix based on a hyaluronic acid derivative is preferably loaded in vitro with autologous and/or allogenic chondrocytes, thus resulting in what has been referred to as *in vitro* cartilage tissue. Therefore, the phrase simply indicates that the non-woven matrix (a) is loaded in vitro with cells (b), thus making said tissue. Consequently, the rejection is deemed overcome and should be withdrawn.

Claims 55 and 58 have been amended in order to overcome the Examiner’s rejection.

It should also be noted that no new matter has been added in amending the claims.

The rejection under § 112, 2nd paragraph, has been overcome and should be withdrawn.

In the outstanding Office Action, the Examiner has rejected claims 51 – 62 under 35 U.S.C. 103(a) as being unpatentable over Angele et al. (US 6,737,072). This rejection is respectfully traversed.

In order to overcome the § 103(a) rejection, Applicants now submit an amended set of claims wherein the surgical method of independent claim 51 has been amended by reciting that the three-dimensional matrix (a) which is based on a hyaluronic acid derivative is in the form of a non-woven tissue and is selected from the class of hyaluronic acid benzyl esters having a percentage of esterification ranging from 75 to 100%. Claim 51 incorporates former claims 61 and 62.

The Examiner states that “Angele et al. teaches methods for repairing (recovering and protecting) musculoskeletal defects (abstract), comprising implanting a matrix (biological material) (abstract) comprising hyaluronic acid esters such as benzyl esters (col.2 line 58-67) and chondrocytes and/or mesenchymal stem cells (col.4, line 7-13).”

Applicants respectfully traverse this interpretation of the cited prior art.

As a matter of fact, Angele et al. indeed teach a **porous composite** matrix comprising a hyaluronic acid derivative **and** a hydrolyzed collagen, in a weight ratio range of hyaluronic acid derivative to hydrolyzed collagen of 30:70 to 99:1 (see Abstract, Summary of the Invention and Claim 1), preferably 70:30 (column 2, lines 20-23). This is further confirmed at column 3, lines 18-40, where the diameter ranges of the pores present in said matrix are discussed.

Therefore, one of ordinary skill in the art at the time the invention was made, is only made aware from Angele et al. of a matrix that is porous **and** composite by involving as essential the combination of a hyaluronic acid derivative **and** a hydrolyzed collagen. No teaching can be found in Angele et al. which addresses, or even only suggests, the possibility to set aside the essential use of said hydrolyzed collagen as well as the possibility of using a non-porous matrix. Notwithstanding this, let us assume

hypothetically, that the Examiner's view of Angele et al. is followed, the skilled person would have to absolutely disregard the comprehensive and actual teaching of Angele et al., take some features entirely out of context while ignoring other features, thus achieving the claimed invention, absent any technical reason to do so.

The Applicants are of the opinion that the Examiner has arbitrarily isolated features from Angele et al. in order to conveniently lead to the claimed invention. This is a clear case of **hindsight reconstruction of the claimed invention** which is not permitted.

Furthermore, the Examiner has acknowledged that the intended use of the claimed invention is not disclosed in Angele et al., nevertheless affirming that "the intended use of the claimed composition does not patentably distinguish the composition, per se, since such undisclosed use is inherent in the reference composition. In order to be limiting, the intended use must create a structural difference between the claimed composition and the composition of the prior art. In the instant case, the intended use fails to create a structural difference, thus, the intended use is not limiting."

In this regard, it should be noted that the current application claims a surgical method designed for a specific body part, i.e. joint cartilage, affected by a peculiar pathology, i.e. osteoarthritis, psoriatic or rheumatoid arthritis, associated with the production of IL-1, by implanting a graft having a defined matrix.

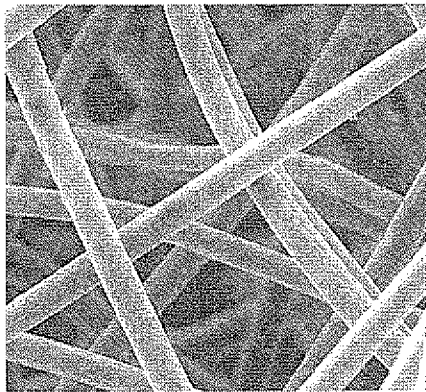
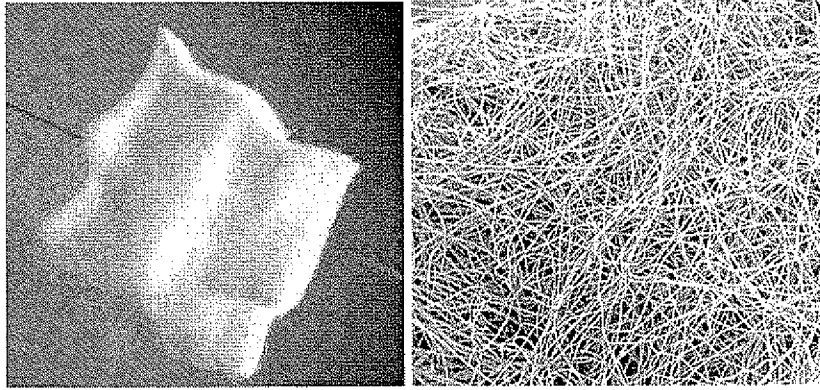
Therefore, this is not the case of a "composition for use ... comprising ...", wherein the intended use has a non-limiting effect unless at least a structural difference in the composition itself makes the same different from known compositions and "suitable for" the cited use.

Applicants are of the opinion that the rejection by the Examiner is based on a misinterpretation of the paragraph "PREAMBLE STATEMENTS RECITING PURPOSE OR INTENDED USE", MPEP 2111.02 Effect of Preamble [R-3], which is not applicable to the present case.

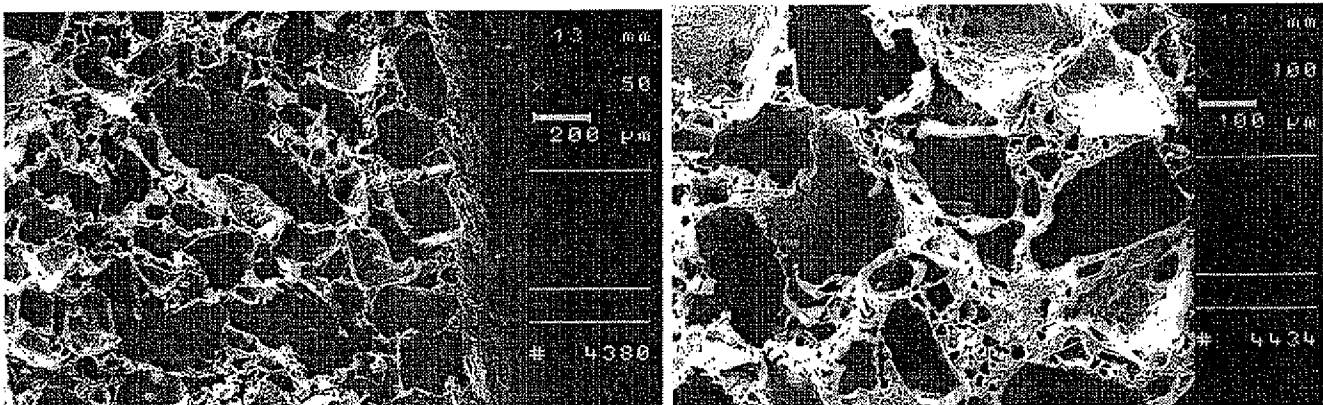
In any event, not only is the biological material of Claim 51 as currently amended structurally different and hence distinguishable from the porous composite matrix of

Angele et al., as above discussed, but also the surgical method of Claim 51 is definitely not recognizable in Angele et al., as already acknowledged by the Examiner herself.

The above mentioned structural differences are even more evident from the following Figures:



where the non-woven matrix of the claimed invention is shown at different magnifications; and



where the porous composite matrix of Angele et al. is shown at different magnifications. (Figure 1 and 2 of the corresponding PCT application, respectively.)

Insofar as the selected degenerative and/or inflammatory pathologies, associated with the production of IL-1 are concerned, Applicants wish to underscore that these pathologies have a peculiar etiology and particular onset conditions that cause the degradation of the cartilage, as reported in the annexed Document A, which is an extract of Cecil Textbook of Medicine, by Wyngaarden and Smith, 1988, W.B. Saunders, pages 433 and 446, all. From this text, the skilled person, at the time the invention was made, was well aware that in a synovial capsule damaged by one of said pathologies, a very high content of pro-inflammatory cytokines are present severely damaging the chondrocytes.

In Angele et al., possible applications of the disclosed porous composite matrix are only generally addressed (column 6, lines 29-58), but the skilled person is provided with no information whatever concerning the conditions that the matrix will undergo once it is implanted, as well as no information at all concerning the effects/consequences of the environment over time towards the implanted matrix.

It should also be noted that in the present application surprising results have been reported demonstrating that the biological material of the invention, once implanted according to the claimed surgical method, shows a strong protective action on the extracellular cartilage matrix when the latter is exposed to the erosive action of pro-inflammatory cytokines that have been over-produced in phlogogenic situations, such as those that occur in the course of osteoarthritis, rheumatoid arthritis and psoriatic arthritis (see par. 0094).

Therefore, Applicants are convinced and respectfully submit that amended claim 51, as well as the dependent claims, clearly distinguishes over Angele et al. by a preponderance of the evidence. Since the Examiner has failed to establish a *prima facie* case of obviousness, the rejection has been overcome and should be withdrawn.

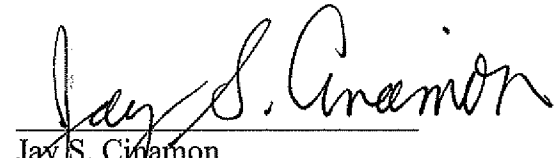
In view of the foregoing, the issuance of a Notice of Allowance is respectfully solicited.

Please charge any fees which may be due and which have not been submitted
herewith to our Deposit Account No. 01-0035.

Respectfully submitted,

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